L Number	Hits	Search Text	DB	Time stamp
1	3794	quinazolin or quinazolinyl	USPAT;	2002/10/24 16:33
			US-PGPUB	
2	7745	quinolin or quinolinyl	USPAT;	2002/10/24 16:33
			US-PGPUB	İ
3	9749	(quinazolin or quinazolinyl) or (quinolin or quinolinyl)	USPAT;	2002/10/24 16:33
			US-PGPUB	
4	500	((quinazolin or quinazolinyl) or (quinolin or quinolinyl))	USPAT;	2002/10/24 16:34
		and (allenylene or vinylene or ethynylene or butadien)	US-PGPUB	
5	469	(((quinazolin or quinazolinyl) or (quinolin or quinolinyl))	USPAT;	2002/10/24 16:35
		and (allenylene or vinylene or ethynylene or butadien)) and	US-PGPUB	
		amino		

EAST 9/914,323

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NEWS WWW

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0.21

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STRUCTURE FILE UPDATES: 23 OCT 2002 HIGHEST RN 464874-85-9 DICTIONARY FILE UPDATES: 23 OCT 2002 HIGHEST RN 464874-85-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Uploading 09914323.str

L1STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1

STR

G1 C, N

G2 O, N

G3 SO2, [@1]

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 16:26:18 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1447 TO ITERATE

69.1% PROCESSED 1000 ITERATIONS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

42 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS:

26659 TO 31221

PROJECTED ANSWERS:

748 TO 1682

L2 42 SEA SSS SAM L1

=> s l1 ful

FULL SEARCH INITIATED 16:26:25 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 28557 TO ITERATE

100.0% PROCESSED 28557 ITERATIONS

1020 ANSWERS

SEARCH TIME: 00.00.04

L3 1020 SEA SSS FUL L1

=> s 13 and (allenyl? or vinyl? or butadien? or ethynyl?)

202 ALLENYL?

65374 VINYL?

45326 BUTADIEN?

81398 ETHYNYL?

L4 19 L3 AND (ALLENYL? OR VINYL? OR BUTADIEN? OR ETHYNYL?)

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST

157.42 157.63

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FILE COVERS 1907 - 24 Oct 2002 VOL 137 ISS 17 FILE LAST UPDATED: 23 Oct 2002 (20021023/ED)

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=> s 14L5 9 L4

=> d 15 1- ibib abs hitstr YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y

ANSWER 1 OF 9 CAPLUS COPYRIGHT 2002 ACS 2002:658094 CAPLUS

ACCESSION NUMBER: DOCUMENT NUMBER:

137:185509

TITLE:

Preparation of 4-phenylaminoquinazoline derivatives as

inhibitors of tyrosine-specific protein kinase

INVENTOR(S):

Kitano, Yasunori; Kawahara, Eiji; Suzuki, Tsuyoshi; Abe, Daisuke; Nakajou, Masahiro; Ueda, Naoko

Mitsubishi Pharma Corporation, Japan PATENT ASSIGNEE(S):

SOURCE:

PCT Int. Appl., 154 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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KIND DATE
                                         APPLICATION NO. DATE
    PATENT NO.
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                                         -----
    WO 2002066445
                     A1 20020829
                                        WO 2002-JP1575 20020221
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
            LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
            PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
            UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                       JP 2001-45827 A 20010221
                                       JP 2001-353525 A 20011119
OTHER SOURCE(S):
                       MARPAT 137:185509
```

GI

#### \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Compds. represented by the following general formula (I) or pharmaceutically acceptable salts thereof, hydrates or solvates of the same or mixts. of optically active isomers, racemic compds. or diastereomers of the same [n = an integer of 0-3; R1 = H, halo, HO, cyano, NO2, CF3, C1-5 alkyl, C1-5 alkoxy, S(0)f-C1-5 alkyl (wherein f = aninteger of 0-2), (un) substituted NH2; one of R2 and R2 is R27SO2NH, (R28SO2)2N, C1-5 alkoxy, MeCOCH2CONH, MeSCH2CH2OCONH, or NCCH2CONH, etc. (wherein R27, R28 = optionally morpholino-substituted C1-5 alkyl) and the other one represents Y(CR12R13)mCR8R9C.tplbond.C, Y(CR12R13)mCR8R9CH:CH, Q, Q1 (wherein R8, R9 = H, optionally HO- or C1-5 alkoxy substituted C1-5 alkyl, or CR8 R9 together represent CO or C3-8 cycloalkylene optionally interrupted by O, S, NH, or alkyl-N; Y = H,HO, C1-5 alkoxy, C1-5 alkanoyloxy, etc.; R11, R12 = H, C1-5 alkyl; m = an integer of 0-3; p, q =2,3; Z = 0, S, S0, S02, CO, optionally substituted NH; p1, p2 = an integer of 1-3; n1 = 0.1; W = H,HO, C1-5 alkoxy, C1-5 alkanoyloxy, C02H, cyano, di-C1-5 alkyamino, morpholino, etc.)] are prepd. These compds. have an

excellent protein kinase inhibitory activity specific to tyrosine and, therefore, are usable as drugs, in particular, remedies/preventives for various cancers, diseases caused by arteriosclerosis or psoriasis. Thus, 1-(1,1-dimethyl-2-propynyl)-4-methylpiperazine was treated with 4,4,5,5-tetramethyl-1,3,2-dioxaborane in the presence of PhCl(PPh3)3 in THF/CH2Cl2 at room temp. and coupled with 4-(3-chloro-4-fluorophenylamino)-6-methoxy-7-quinazolinyl triflate (prepn. given) in the presence of PdCl2(dppf).CH2Cl2 [dppf = 1,1'-bis(diphenylphosphino)ferrocene] in a mixt. of DMF and 2 m aq. Na2CO3 80.degree. for 1 h to give the title compd. (II). II.HCl showed IC50 of 0.82 nM against EGF receptor tyrosine kinase.

IT 451493-01-9P 451494-03-4P 451494-18-1P 451494-25-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of phenylaminoquinazoline derivs. as inhibitors of tyrosine-specific protein kinase for prepn. and/or treatment of cancers, diseases caused by arteriosclerosis, or psoriasis)

RN 451493-01-9 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[1-(4-methyl-1-piperazinyl)cyclohexyl]ethynyl]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

RN 451494-03-4 CAPLUS

CN

Methanesulfonamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[1-(4-methyl-1-piperazinyl)cyclohexyl]ethynyl]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

RN 451494-18-1 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[tetrahydro-4-(4-methyl-1-piperazinyl)-2H-pyran-4-yl]ethynyl]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

RN 451494-25-0 CAPLUS CN 2-Propenamide, N-[4-

2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[4-(diethylamino)-

4-piperidinyl]ethynyl]-6-quinazolinyl]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 451494-24-9 CMF C28 H30 Cl F N6 O

$$C = C - R$$

CM 2

CRN 76-05-1 CMF C2 H F3 O2

#### IT 451494-23-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of phenylaminoquinazoline derivs. as inhibitors of tyrosine-specific protein kinase for prepn. and/or treatment of cancers, diseases caused by arteriosclerosis, or psoriasis)

RN 451494-23-8 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[4-[(3-chloro-4-fluorophenyl)amino]-6-[(1-oxo-2-propenyl)amino]-7-quinazolinyl]ethynyl]-4-(diethylamino)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

$$C = C - R$$

$$C = C - R$$

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:693148 CAPLUS

DOCUMENT NUMBER:

135:242152

TITLE:

Preparation of 4-anilinoquinoline-3-carbonitriles as

colonic polyp inhibitors

INVENTOR(S):

Frost, Philip; Discafani-Marro, Carolyn M.

PATENT ASSIGNEE(S):

American Cyanamid Company, USA PCT Int. Appl., 207 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.				KIND		DATE			APPLICATION NO.					DATE				
WO	2001068186			A2		20010920		W	20	01-U	S706	8	20010306					
WO	2001	2001068186		A3		20020117												
	W:	ΑE,	AG,	ΑL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
														GD,				
														LC,				
														NZ,				
			_											UA,				
		YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM	,	-		•	
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,	
														PT,			-	
		ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG	•	-	
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PRIORITY APPLN. INFO.:								τ	JS 2	000-	3041	98P	P	2000	0313			
								τ	JS 20	000-	5241	96	Α	2000	0313			
OTHER SOURCE(S) ·					MAR	י דעם	135.1	2421	52									

OTHER SOURCE(S): MARPAT 135:242152

GI

AB R(CH2)nZZ1CN [I; R = (un)substituted cycloalkyl, -Ph, -pyridinyl, -pyrimidinyl; Z = O, S, (alkyl)imino; Z1 = 5-8-(un)substituted quinoline-4,3-diyl; n = 0 or 1] were prepd. Thus, 3-(MeO)C6H4NH2 was cyclocondensed with NCC(:CHOEt)CO2Et and the chlorinated product aminated by 3-BrC6H4NH2 to give title compd. II. Data for biol. activity of 1 prepd. I were given.

IT 214485-23-1P 214485-24-2P 214485-25-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 4-anilinoquinoline-3-carbonitriles as colonic polyp inhibitors)

RN 214485-23-1 CAPLUS

CN 2-Butynamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]- (9CI) (CA INDEX NAME)

RN 214485-24-2 CAPLUS

CN 2-Propenamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]- (9CI) (CA INDEX NAME)

$$H_2C = CH - C - NH$$
 $CN$ 
 $NH$ 
 $NH$ 

RN 214485-25-3 CAPLUS

CN 2-Butynamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]-4-(1-piperidinyl)- (9CI) (CA INDEX NAME)

L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:185 CAPLUS

DOCUMENT NUMBER:

134:207783

TITLE:

Tyrosine kinase inhibitors. 18. 6-Substituted 4-anilinoquinazolines and 4-anilinopyrido[3,4-

d]pyrimidines as soluble, irreversible inhibitors of

the epidermal growth factor receptor

AUTHOR (S):

Smaill, Jeff B.; Showalter, H. D. Hollis; Zhou, Hairong; Bridges, Alexander J.; McNamara, Dennis J.; Fry, David W.; Nelson, James M.; Sherwood, Veronika; Vincent, Patrick W.; Roberts, Bill J.; Elliott,

William L.; Denny, William A.

CORPORATE SOURCE:

Auckland Cancer Society Research Centre Faculty of Medicine and Health Science, The University of

Auckland, Auckland, 92019, N. Z.

SOURCE:

Journal of Medicinal Chemistry (2001), 44(3), 429-440

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

GI

# \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB 4-Anilinoquinazoline- and 4-anilinopyrido[3,4-d]pyrimidine-6-acrylamides are potent pan-erbB tyrosine kinase inactivators, and one example (CI-1033) is in clin. trial. A series of analogs with a variety of Michael acceptor units at the 6-position, I [X = N, C, R1 = H, Me](CH2) 2NMe2, etc., R2 = H, Me, R3 = H, cis-Cl, CF3, etc.], II, and III ( $X = \frac{1}{2}$ ) N, C, R1 = NHSO2CH:CH2, SO2CH2CH2OH, SO2CH:CH2, SOCH:CH2), were prepd. to define the structural requirements for irreversible inhibition. A particular goal was to det. whether addnl. functions to increase soly. could be appended to the Michael acceptor. Substituted acrylamides were prepd. by direct acylation of the corresponding 6-amines with the requisite acid or acid chloride. Vinylsulfonamide derivs. were obtained by acylation of the amines with chloroethylsulfonyl chloride followed by base-promoted elimination. Vinylsulfone and vinylsulfine derivs. were prepd. by oxidn. and base elimination of a hydroxyethylthio intermediate. The compds. were evaluated for their inhibition of phosphorylation of the isolated EGFR enzyme and for inhibition of EGF-stimulated autophosphorylation of EGFR in A431 cells and of heregulin-stimulated autophosphorylation of erbB2 in MDA-MB 453 cells. Substitution at the nitrogen of the acrylamide was tolerated only with a Me group; larger substituents were dystherapeutic, and no substitution at all was tolerated at the acrylamide .alpha.-carbon. In contrast, while electron-donating groups at the acrylamide .beta.-carbon were not useful, even quite large electron-withdrawing groups (which increase its electrophilicity) were tolerated. A series of derivs. with soly.-enhancing substituents linked to the acrylamide .beta.-carbon via amides were potent irreversible inhibitors of isolated EGFR (IC50s = 0.4-1.1 nM), with weakly basic morpholine and imidazole derivs. being the best. Vinylsulfonamides were also potent and irreversible inhibitors, but vinylsulfones and vinylsulfines were reversible and only poorly active. Two compds. were evaluated against A431, H125, and MCF-7 xenografts in nude mice but were inferior in these assays to the clin. trial compd. CI-1033.

IT 198960-23-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn., epidermal growth factor receptor inhibitory activity, and structure-activity relationship of anilinoquinazolines and -pyridopyrimidines)

RN 198960-23-5 CAPLUS

CN 2,3-Butadienamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1999:794373 CAPLUS

DOCUMENT NUMBER: 132:35620

TITLE: Preparation of substituted 3-cyanoquinolines as

inhibitors of growth factor receptor protein tyrosine

kinases (PTK)

INVENTOR(S): Wissner, Allan; Johnson, Bernard D.; Reich, Marvin F.;

Floyd, Middleton B. , Jr.; Kitchen, Douglas B.; Tsou,

Hwei-ru

PATENT ASSIGNEE(S): American Cyanamid Co., USA

SOURCE: U.S., 80 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

US 6002008 A 19991214 US 1998-49718 19980327

PRIORITY APPLN. INFO.: US 1997-41963P P 19970403

OTHER SOURCE(S): MARPAT 132:35620

GI

$$R^{2}$$
 $R^{2}$ 
 $R^{3}$ 
 $R^{4}$ 
 $R^{2}$ 
 $R^{3}$ 
 $R^{4}$ 
 $R^{2}$ 
 $R^{3}$ 
 $R^{4}$ 
 $R^{2}$ 
 $R^{3}$ 

AΒ This invention provides compds. having the formula (I; wherein: X is cycloalkyl which may be optionally substituted; or is a pyridinyl, pyrimidinyl, or Ph ring; wherein the pyridinyl, pyrimidinyl, or Ph ring may be optionally substituted; n is 0-1; Y is NH, O, S, or NR; R is alkyl of 1-6 carbon atoms; R1, R2, R3, and R4 are each, independently, hydrogen, halogen, alkyl, alkenyl, alkenyl, alkenyloxy, alkynoyloxy, hydroxymethyl, halomethyl, alkanoyloxy, alkenoyloxy, alkynyloxy, alkanoyloxymethyl, alkenoyloxymethyl, alkoxymethyl, alkoxy, alkylthio, alkylsulphinyl, alkylsulfonyl, alkylsulfonamido, alkenylsulfonamido, alkynylsulfonamido, hydroxy, trifluoromethyl, cyano, nitro, carboxy, carboalkoxy, carboalkyl, phenoxy, Ph, thiophenoxy, benzyl, amino, hydroxyamino, alkoxyamino, alkylamino, dialkylamino, aminoalkyl, N-alkylaminoalkyl, N,N-dialkylaminoalkyl, phenylamino, benzylamino, etc.; R5 is alkyl which may be optionally substituted, or Ph which may be optionally substituted; R6 is hydrogen, alkyl, or alkenyl; R7 is chloro or bromo; R8 is hydrogen, alkyl, aminoalkyl, N-alkylaminoalkyl, N, N-dialkylaminoalkyl, N-cycloalkylaminoalkyl, N-cycloalkyl-Nalkylaminoalkyl, N,N-dicycloalkylaminoalkyl, morpholino-N-alkyl, piperidino-N-alkyl, N-alkyl-piperidino-N-alkyl, azacycloalkyl-N-alkyl, hydroxyalkyl, alkoxyalkyl, carboxy, carboalkoxy, Ph, carboalkyl, chloro, fluoro, or bromo; Z is amino, hydroxy, alkoxy, alkylamino, dialkylamino). The compds. of the present invention inhibit the action of certain growth factor receptor protein tyrosine kinases (PTK) thereby inhibiting the abnormal growth of certain cell types. They are therefore useful for the treatment of certain diseases that are the result of deregulation of these PTKs, in particular as anti-cancer agents for the treatment of cancers expressing epidermal growth factor receptor (EGFR), mitogen activated protein kinase (MAPK), epithelial kinase (ECK), and kinase insert domain contg. receptor (KDR) in mammals and for the treatment of polycystic kidney disease in mammals. Thus, To a mixt. of 1.9 g (5.1 mmol) of 4-[(3-bromopheny1)amino]-7-methoxy-6-amino-3-quinolinecarbonitrile and 5.3 mL (31 mmol) of Hunig's base in 110 mL of dry THF at 0.degree. C., with stirring, was added a THF soln. contg. 5.7 g (31 mmol) of 4-bromocrotonyl chloride dropwise. The mixt. was stirred for addnl. 0.5 h. After addn. 100 mL of satd. sodium chloride soln. was added to the reaction mixt., then it was extd. with Et acetate. The Et acetate soln. was dried over

sodium sulfate and then was added to 40 mL of di-Me amine soln. (2.0 M in THF) at 0.degree. dropwise and stirred an addnl. 0.5 h to give 4-Dimethylamino-but-2-enoic acid [4-(3-bromo-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]amide (II). II showed IC50 of 0.000008 .mu.M against epidermal growth factor receptor kinase.

IT 214485-23-1P 214485-24-2P 214485-25-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of substituted 3-cyanoquinolines as inhibitors of growth factor receptor protein tyrosine kinases (PTK) for treatment of cancers and polycystic kidney disease)

RN 214485-23-1 CAPLUS

CN 2-Butynamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]- (9CI) (CA INDEX NAME)

$$Me-C = C-C-NH$$

$$NH$$

$$NH$$

$$NH$$

RN 214485-24-2 CAPLUS

CN 2-Propenamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]- (9CI) (CA INDEX NAME)

RN 214485-25-3 CAPLUS

CN 2-Butynamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]-4-(1-piperidinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & O \\
 & N \\
 & CH_2 - C \\
 & C \\
 & C \\
 & NH
\end{array}$$

$$\begin{array}{c}
 & O \\
 & NH \\
 & CN
\end{array}$$

$$\begin{array}{c}
 & NH \\
 & NH \\
 & CN
\end{array}$$

REFERENCE COUNT:

29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 5 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1999:113656 CAPLUS

DOCUMENT NUMBER:

130:168387

TITLE:

Irreversible inhibitors of tyrosine kinases

INVENTOR(S): PATENT ASSIGNEE(S): Bridges, Alexander James Warner-Lambert Company, USA

SOURCE:

PCT Int. Appl., 124 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

```
PATENT NO.
                                              APPLICATION NO. DATE
                       KIND
                             DATE
                                               -----
                              19990211
                                              WO 1998-US15784 19980729
     WO 9906378
                        A1
         W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG,
              SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD,
         RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
              FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
              CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9887607
                        A1
                              19990222
                                              AU 1998-87607
                                                                 19980729
     US 6127374
                         Α
                              20001003
                                              US 1999-269545
                                                                 19990325
PRIORITY APPLN. INFO.:
                                           US 1997-54060P P
                                                                 19970729
                                           WO 1998-US15784 W 19980729
                          MARPAT 130:168387
```

OTHER SOURCE(S):

Pyrimidine derivs. that are irreversible inhibitors of tyrosine kinases are reported. Thus, PhCH2OH was treated with 4-FC6H4NO2 to give 4-PhCH2OC6H4NO2, which was reduced to the amine and used to aminate 4-chloro-6-nitroquinazoline hydrochloride. The resulting 6-nitro-4-(4-benzyloxyanilino)quinazoline hydrochloride was reduced to the amine and acylated to give N-[4-(4-benzyloxyanilino)quinazolin-6yl]acrylamide (I). I had an IC50 for inhibition of epidermal growth factor receptor tyrosine kinase of 3.6 nM.

IT 220488-36-8P 220488-37-9P 220489-67-8P

220489-69-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of anilinoquinazolinylacrylamides and related compds. as tyrosine kinase inhibitors)

RN 220488-36-8 CAPLUS

CN 2,3-Butadienamide, N-[4-[(4-phenoxyphenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

$$H_2C = C = CH - C - NH$$

NH

OPh

RN 220488-37-9 CAPLUS

CN 2,3-Butadienamide, N-[4-[[4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]-(9CI) (CA INDEX NAME)

$$H_2C = C = CH - C - NH$$
 $NH$ 
 $NH$ 
 $Ph - CH_2 - O$ 

RN 220489-67-8 CAPLUS

CN 2,3-Butadienamide, N-[4-[[4-(phenylmethyl)phenyl]amino]-6-quinazolinyl](9CI) (CA INDEX NAME)

RN 220489-69-0 CAPLUS

CN 2,3-Butadienamide, N-[4-[[3-chloro-4-[(1-methyl-1H-imidazol-2-yl)thio]phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

$$H_2C = C = CH - C - NH$$
 $NH$ 
 REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 6 OF 9 CAPLUS COPYRIGHT 2002 ACS 1998:682233 CAPLUS ACCESSION NUMBER:

129:302564 DOCUMENT NUMBER:

TITLE: Preparation of substituted 3-cyanoquinolines as

inhibitors of protein tyrosine kinase

Wissner, Allan; Johnson, Bernard Dean; Reich, Marvin INVENTOR(S):

Fred; Floyd, Middleton Brawner, Jr.; Kitchen, Douglas

B.; Tsou, Hwei-ru

PATENT ASSIGNEE(S): American Cyanamid Co., USA

SOURCE: PCT Int. Appl., 223 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE:

English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE \_ \_ \_ \_ ----------A1 19981008 WO 9843960 WO 1998-US6480 19980402 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG CN 1161330 Α 19971008 CN 1997-101099 19970204 ZA 9802771 Α 19991001 ZA 1998-2771 19980401 AU 9868777 **A1** 19981022 AU 1998-68777 19980402 AU 750906 B2 20020801 EP 973746 **A**1 20000126 EP 1998-914417 19980402 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO JP 2001519788 T2 20011023 JP 1998-541981 19980402 NO 9904798 19991124 NO 1999-4798 19991001 PRIORITY APPLN. INFO.: US 1997-826604 A 19970403 WO 1998-US6480 W 19980402

OTHER SOURCE(S): MARPAT 129:302564

GΙ

$$\begin{array}{c|c}
R^1 & \text{CH}_2|_{n} X \\
R^2 & \text{CN} \\
R^3 & R^4
\end{array}$$

The title compds. [I; X = (un)substituted cycloalkyl, pyridinyl, pyrimidinyl, Ph; n = 0-1; Y = NH, O, S, NR; R = = C1-6 alkyl; R1-R4 = H, halo, alkyl, etc. (with the proviso that when Y = NH; R1-R4 = H; n = O; X is not 2-methylphenyl)], inhibitors of protein tyrosine kinase which are useful in treating, inhibiting the growth of, or eradicating a neoplasm which expresses EGFR, MAPK, ECK or KDR, and in treating polycystic kidney disease, were prepd. Thus, treatment of 2-butynoic acid with iso-Bu chloroformate and N-methylmorpholine in THF followed by the addn. of this soln. of the mixed anhydride to a soln. of 6-amino-4-[(3-bromophenyl)amino]-7-methoxy-3-quinolinecarbonitrile (prepn. described) in THF over a 24 h period afforded I [Y = NH; n = 0; X = 3-BrC6H4; R1 = R4 = H; R2 = MeC.tplbond.CC(O)NH; R3 = MeO] which showed IC50 of 0.15 .mu.M against epidermal growth factor receptor kinase (A431 membrane ext.).

IT 214485-23-1P 214485-24-2P 214485-25-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

Ι

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of substituted 3-cyanoquinolines as inhibitors of protein tyrosine kinase)

RN 214485-23-1 CAPLUS

CN 2-Butynamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]- (9CI) (CA INDEX NAME)

$$Me-C = C-C-NH$$

$$NH$$

$$NH$$

$$NH$$

RN 214485-24-2 CAPLUS

CN 2-Propenamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]- (9CI) (CA INDEX NAME)

RN 214485-25-3 CAPLUS

2-Butynamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]-4-(1-CN piperidinyl) - (9CI) (CA INDEX NAME)

REFERENCE COUNT: THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS 6 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1998:282401 CAPLUS

DOCUMENT NUMBER:

128:321653

TITLE: Preparation of alkynyl- and azido-substituted

4-anilinoquinazolines for the treatment of

hyperproliferative diseases

INVENTOR(S): Schnur, Rodney Caughren; Arnold, Lee Daniel

PATENT ASSIGNEE(S): Pfizer Inc., USA SOURCE: U.S., 23 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE US 5747498 19980505 US 1996-653786 19960528 OTHER SOURCE(S): CASREACT 128:321653; MARPAT 128:321653

GΙ

$$\begin{bmatrix} \mathbb{R}^{2} \end{bmatrix}_{\mathbb{N}} \mathbb{R}^{4}$$

AB The title compds. [I; R1 = H, halo, OH, etc.; R2 = H, (un)substituted C1-6 alkyl; R3 = H, halo, OH, etc.; R4 = N3, (un)substituted ethynyl; m = 1-3; n = 1-2] and their salts, useful in the treatment of hyperproliferative diseases such as cancer, were prepd. Thus, reaction of 4-chloro-6,7-dimethoxyquinazoline with 4-azidoaniline hydrochloride in iPrOH afforded 98% I [R1 = 6,7-Me2; R2, R3 = H; R4 = 4-N3]. Compds. I showed IC50 of 0.0001-30 .mu.M against EGFR kinase.

IT 183319-40-6P 183319-48-4P 183319-51-9P 183321-68-8P 183321-69-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of alkynyl- and azido-substituted 4-anilinoquinazolines for the treatment of hyperproliferative diseases)

RN 183319-40-6 CAPLUS

CN Methanesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

RN 183319-48-4 CAPLUS

CN Benzenesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

# ● HCl

RN 183319-51-9 CAPLUS

CN 2H-Isoindole-2-ethanesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-1,3-dihydro-1,3-dioxo-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & O & O & N \\
 & N - CH_2 - CH_2 - S - NH - NH \\
 & O & NH
\end{array}$$

## ● HCl

RN 183321-68-8 CAPLUS

CN Benzenesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-4-methyl-(9CI) (CA INDEX NAME)

RN 183321-69-9 CAPLUS

CN 2H-Isoindole-2-ethanesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-1,3-dihydro-1,3-dioxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & O \\
 & N \\
 & CH_2 - CH_2 - S \\
 & O \\$$

ANSWER 8 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: DOCUMENT NUMBER:

1997:696745 CAPLUS 128:3695

TITLE:

Preparation of N-quinazolinylacrylamides and analogs

as tyrosine kinase inhibitors

INVENTOR (S):

Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong; et

al.

PATENT ASSIGNEE(S):

Warner-Lambert Company, USA; Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis;

Smaill, Jeffrey B.; Zhou, Hairong

SOURCE:

PCT Int. Appl., 193 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	PATENT NO.			KI	ND	DATE APPLI					CATION NO.			DATE				
WO	9738983			A1 19971023				WO 1997-US5778						19970408				
	W:	AL,	ΑU,	BA,	BB,	ВG,	BR,	CA,	CN,	CZ,	EE,	GΕ,	GH,	HU,	IL,	IS,	JP,	
		KR,	LC,	LK,	LR,	LT,	LV,	MG,	MK,	MN,	MX,	NO,	NZ,	PL,	RO,	SG,	SI,	
		SK,	TR,	TT,	UA,	US,	UZ,	VN,	YU,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM
	RW:													ES,				
		GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	
		ML,	MR,	ΝE,	SN,	TD,	TG											
CA	2249	446		A	A	1997	1023		CZ	A 19	97-2	2494	46	1997	0408			
	9724								ΑŢ	J 19	97-2	4463		1997	0408			
AU	7255	33		B:	2	2000	1012											
EP	8927	892789		A:	Al 19990127				EP 1997-920213			3	19970408					
EP	8927	89		B	1	2002	0227											
	R:	ΑT,	ΒE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
				LT,														
	1218																	
	9708																	
JP	2000	5086!	57	T:	2	2000	0711		JI	19:	97-5	3717	3	19970	0408			
	2137																	
	9703																	
	9804																	
KR	2000	0053	64	Α		2000	0125		KI	19:	98-8	086		1998	1010			
KR	2000	00536	54	Α		2000	0125		KI	199	98-7	08086	6	1998	1010			
	6344													19990				
PRIORIT	Y APP	LN.	INFO	.:				Ţ	JS 19	96-1	1535	1P	P	19960	1412			

WO 1997-US5778 W 19970408

OTHER SOURCE(S):

MARPAT 128:3695

GI

Title compds. [I; R = (CHR6)pR9; R1R2 = CH:CR7CR8:CH, CH:CR7CR8:N, CH:CR7N:CH, etc.; R6 = H or alkyl; 1 of R7,R8 = Z1ZZR10 and the other = OR4, SR4, NHR3; R3,R4 = (un)substituted alkyl, heterocyclylalkyl, etc.; R9 = (un)substituted Ph; R10 = CR11:CHR5, C.tplbond.CR5, CR11:C:CHR5; R5 = H, halo, alkyl, Ph, etc.; R11 = H, halo, alkyl; Z1 = bond, O, (alkyl)imino, CH2, etc.; Z2 = CO, SO, P(O)(OH), etc.; p = 0 or 1] were prepd. Thus, I (R = C6H4Br-3, R1R2 = CH:NCR8:CH, R8 = F) was condensed with 3-morpholinoprpanamine and the product acylated by CH2:CHCOCl to give title compd. II. Data for biol. activity of I were given.

IT 198960-23-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-quinazolinylacrylamides and analogs as tyrosine kinase inhibitors)

RN 198960-23-5 CAPLUS

CN 2,3-Butadienamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:701606 CAPLUS

DOCUMENT NUMBER: 125:328728

TITLE: Preparation of N-phenylquinazoline-4-amines as

neoplasm inhibitors

INVENTOR(S): Schnur, Rodney C.; Arnold, Lee D.

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	PATENT NO.			DATE	ATE APPLICATION NO					
						WO 1995-IB436				
	W: CA	, FI,	JP, MX	, US						
						B, GR, IE, IT,				SE
CA	2216796		AA	19961003		CA 1995-22167 EP 1995-91871	96	19950606		
EP	817775		A1	19980114		EP 1995-91871	3	19950606		
				20010912						
	R: AT	, BE,	CH, DE	, DK, ES,	FR, G	B, GR, IT, LI,	LU	, NL, SE,	PT,	ΙE
JР	1050663	3	T2	19980630		JP 1995-52911	3	19950606		
JР	3088018		B2	20000918		JP 1996-52911	3	19950606		
						EP 2001-10469				
	R: AT	, BE,	CH, DE	, DK, ES,	FR, G	B, GR, IT, LI,	LU	, NL, SE,	PT,	ΙE
AT	205483		E	20010915		AT 1995-91871 ES 1995-91871 TW 1996-85102 CN 1996-10299	3	19950606		
ES	2161290		<b>T</b> 3	20011201		ES 1995-91871	3	19950606		
TW	454000		В	20010911		TW 1996-85102	699	19960305		
CN	1137037		Α	19961204		CN 1996-10299	2	19960328		
CN	1066142		В	20010523						
NO	9601299		Α	19961001		NO 1996-1299 AU 1996-50406		19960329		
AU	9650406		<b>A</b> 1	19961010		AU 1996-50406		19960329		
AU	703638		B2	19990325						
ZA	9602522		Α	19970929		ZA 1996-2522		19960329		
BR	9601200		Α	19980106		BR 1996-1200		19960329		
RU	2174977		C2	20011020		RU 1996-10605	5	19960329		
FI	9703832		Α	19970929		FI 1997-3832		19970929		
AU	9935854		A1	19990819		AU 1999-35854		19990623		
PRIORIT	Y APPLN.	INFO	.:		US	1995-413300 1995-918713	A2	19950330		
					EP	1995-918713	<b>A3</b>	19950606		
					WO	1995-IB436 1996-50406	W	19950606		
					AU	1996-50406	A3	19960329		
OTHER C	OTTDOD (C)		147	DDXM 10E.						

OTHER SOURCE(S):

MARPAT 125:328728

$$\mathbb{R}^{\frac{1}{m}} \longrightarrow \mathbb{N} \qquad \mathbb{N}$$

Title compds. [I; r = NR2ZR4; R1 = H, halo, NH2, CO2H, etc.; R2 = HAΒ (un) substituted alkyl; R4 = N3, C.tplbond.CR3; R3 = H, (un) substituted alkyl; Z = (un) substituted phenylene; m = 1-3] were prepd. Thus, 4-chloro-6,7-dimethoxyquinazoline was aminated by 3-(HC.tplbond.C)C6H4NH2 to give title compd. II. I had IC50 of 10-4 to 30.mu.M against phosphorylation on Lys3-gastrin tyrosine by epidermal growth factor receptor kinase in vitro.

IT 183319-40-6P 183319-48-4P 183319-51-9P 183321-68-8P 183321-69-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

RN 183319-48-4 CAPLUS
CN Benzenesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-4-methyl, monohydrochloride (9CI) (CA INDEX NAME)

#### HCl

RN 183319-51-9 CAPLUS
CN 2H-Isoindole-2-ethanesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-1,3-dihydro-1,3-dioxo-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & O & \\
 & N - CH_2 - CH_2 - S - NH - NH \\
 & O & NH
\end{array}$$

## ● HCl

RN 183321-68-8 CAPLUS

CN Benzenesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-4-methyl-(9CI) (CA INDEX NAME)

RN 183321-69-9 CAPLUS

CN 2H-Isoindole-2-ethanesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-1,3-dihydro-1,3-dioxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ N & & CH_2 - CH_2 - S - NH \\ & & & \\ O & & & NH \\ \end{array}$$

=> d his

(FILE 'HOME' ENTERED AT 16:25:32 ON 24 OCT 2002)

FILE 'REGISTRY' ENTERED AT 16:25:40 ON 24 OCT 2002 STRUCTURE UPLOADED

L1 STRUC L2 42 S L1 09/ 914,323

L3 1020 S L1 FUL

L4 19 S L3 AND (ALLENYL? OR VINYL? OR BUTADIEN? OR ETHYNYL?)

FILE 'CAPLUS' ENTERED AT 16:28:14 ON 24 OCT 2002

L5 9 S L4

=> log y

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 41.88 199.51

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION

CA SUBSCRIBER PRICE -5.58 -5.58

STN INTERNATIONAL LOGOFF AT 16:32:04 ON 24 OCT 2002